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Etude par calorimétrie directe et indirecte de l'effet thermique post-prandial chez l'homme

PARTIE DE LA THÈSE

présentée à la Faculté des Sciences
de l'Université de Lausanne
pour l'obtention du grade de docteur ès sciences

par

PHILIPPE G. PITTET
Licencié ès sciences naturelles (diplôme d'Etat)
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IMPRIMATUR

Vu le rapport présenté par le jury d'examen, composé de MM. les professeurs Eric Jéquier, directeur de thèse, P.-E. Pilet, rapporteur de la Faculté, et G. Brunisholz, président du jury, le Conseil de Faculté autorise l'impression de la thèse de M. Philippe G. Pittet, licencié ès sciences naturelles (diplôme d'Etat) de l'Université de Lausanne, intitulée : « Etude par calorimétrie directe et indirecte de l'effet thermique post-prandial chez l'homme ».

Lausanne, le 27 février 1975

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Les tirés à part de Br. J. Nutr. (1974), *31*, 343 et Br. J. Nutr. (1976), *35*, 281, constituent une partie de la thèse présentée, dont un texte dactylographié complet peut être consulté à la Bibliothèque cantonale et universitaire de Lausanne.

Br. J. Nutr. (1976), 35, 281

Thermic effect of glucose in obese subjects studied by direct and indirect calorimetry

By Ph. PITTET, Ph. CHAPPUIS, K. ACHESON, F. de TECHTERMANN and E. JÉQUIER

Division of Clinical Physiology and Institute of Physiology, University of Lausanne, 1011 Lausanne, Switzerland

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1. The thermic effect of a glucose load (50 g) was studied in ten control and eleven obese female subjects, using both direct and indirect calorimetry simultaneously. Experiments were done under conditions of thermal equilibrium (28° and 30% relative humidity).

2. Thermal balance (heat production measured by indirect calorimetry minus heat losses measured directly) was negative in the control group during the fasting period (heat deficit $-14{\cdot}2 \pm 5{\cdot}0$ kJ/m^2 per h), whereas that of the obese group was in equilibrium ($+1{\cdot}4 \pm 4{\cdot}8$ kJ/m^2 per h).

3. After the glucose load, metabolic rate increased $13{\cdot}0 \pm 1{\cdot}5$ and $5{\cdot}2 \pm 1{\cdot}3$% in the control and obese groups respectively.

4. In contrast to the metabolic rate, total heat losses were not significantly altered in either group after the glucose load. Total heat losses of the obese group were significantly lower than those of the control group throughout the experimental period.

5. During the experiments the amount of heat stored was increased in both groups. Thermal balance in the control group became positive while that of the obese group remained positive.

6. During the fasting period, the control subjects oxidized more carbohydrates (90·4 mg/min) than lipids (68·8 mg/min), whereas obese subjects oxidized more lipids (103·7 mg/min) than carbohydrates (50·2 mg/min). After the glucose load, the oxidation rate of carbohydrates was increased in both groups to 158·1 mg/min in control subjects and 95·6 mg/min in obese subjects.

7. The mean skin temperature of the control subjects was significantly higher than that of the obese subjects and remained higher throughout the postprandial period.

8. These results indicate that: (*a*) during the fasting period, the energy sources utilized and the thermal balance of the two groups were different; (*b*) the thermic effect of glucose was less in the obese subjects and, therefore, might be a factor contributing to their low energy expenditure.

It is widely believed that people become obese because they eat relatively more than non-obese individuals. Thus obesity has for many years been attributed to gluttony. However, this is frequently not the situation (Johnson, Burke & Mayer, 1956; Stefanik, Heald & Mayer, 1959).

Many other criteria are involved in the development of obesity: e.g. social, economic and genetic profiles, muscular activity and biochemical characteristics. Galton & Bray (1967) have reported that the activity of the glycerophosphate cycle is reduced in the adipose tissue of obese subjects, suggesting a more efficient use of energy than in control subjects. Miller & Mumford (1966), and Stirling & Stock (1968) suggest that the development of obesity is likely to be due to a thermogenic defect rather than an aberration in appetite, while Linton, Conley, Kuechenmeister & McClusky (1972) suggest that obese individuals take longer to recognize their feeling of satiety and discomfort with continued eating. Cabanac & Duclaux (1970) have also reported a deficiency in the satiety response to sucrose in obese subjects.

Table 1. *Main physical characteristics of the two groups of female subjects used in the study*

(Mean values with their standard errors)

Subjects	*n*	Age (years)	Height (m)	Body surface (m^2)	Body-wt kg	Body-wt % ideal wt
Control	10	24·2 ± 1·7	1·69 ± 2·1	1·63 ± 0·04	56·6 ± 1·9	102·0 ± 2·0
Obese	11	28·9 ± 3·2	1·64 ± 1·7	1·90 ± 0·05	83·7 ± 4·4	159·3 ± 7·9
		NS	NS	***	***	***

NS, not significant.

Differences between mean values for the two groups were statistically significant (unpaired *t* test): *** $P < 0.001$.

The thermic effect of nutrients represents a loss of energy for the body. Since frankly obese subjects can maintain their weight with a lower energy intake than lean subjects, it was of interest to study whether the thermic effect of glucose might be lower in obese subjects than in lean controls.

We studied oxygen consumption, the oxidation rate of lipids, carbohydrates and proteins, total heat losses and thermal balance in two groups of female subjects, after an oral load of 50 g glucose.

EXPERIMENTAL

Two groups of females who were unfamiliar with the equipment were studied in a direct calorimeter as described previously (Pittet, Gygax & Jéquier, 1974).

The first group consisted of eleven obese females, with no evidence of endocrinological disturbances, and the second was a group of ten healthy, lean female subjects. Their main physical characteristics are given in Table 1. Each subject had fasted for 12 h, overnight, and was allowed to rest for 1 h in a constant temperature room at 28° and 30% relative humidity, before measurements were made. The subject, wearing a minimum of underclothing, was introduced into the calorimeter which was regulated to the same ambient conditions as those of the constant temperature room. Initial (fasting) measurements were taken for 40 min or until stable values were obtained. The subject was then given an oral dose of 50 g glucose and the measurements were continued for a further 150 min. The following measurements were made continuously throughout the experiment:

Internal temperature. This was measured using a tympanic and a sublingual probe.

Mean skin temperature. This was estimated by weighting eight different skin temperatures according to the procedure of Hardy & Du Bois (1937).

Metabolic rate and respiratory quotient (RQ). These were estimated from determinations of ventilation, and the concentrations of O_2 and carbon dioxide in the expired air, using an open-circuit system (Gomez, Jéquier, Chabot, Büber & Felber, 1972). Although the RQ can be influenced by changes in ventilation over short periods (i.e. hypo- or hyperventilation) its integration over 30 min periods corrects for these changes and results in a mean RQ which reflects the true oxidation rate of energy substrates.

The amount of protein (estimated in terms of amino acids) metabolized was cal-

culated from the urinary nitrogen excretion (Du Bois, 1924). The 'non-protein' RQ was then determined and the tables of Lusk (1924) were used to compute the amount of carbohydrate and lipid (as fatty acids) oxidized during the experiment. Total heat losses were measured by gradient-layer direct calorimetry (Spinnler, Jéquier, Favre, Dolivo & Vannotti, 1973) which enabled the separate measurement of 'dry' heat losses (radiation + convection) and 'evaporative' heat losses (insensible perspiration and sweating) to be made.

Statistical analyses were done using Student's *t* test for paired and unpaired results. The threshold of significance was $P < 0{\cdot}05$.

RESULTS

Metabolic rate and heat losses

After the glucose load, the metabolic rate, measured over a period of 150 min, increased significantly in both groups (Table 2). In the control group, this increase was 13·0% of the initial (fasting) value, whereas in the obese group it was only 5·2%, i.e. about half the thermic effect found in the control group. This difference in metabolic rate stimulation was highly significant (Table 3).

During the 150 min after the glucose load neither the total nor the 'evaporative' heat losses (which represent about 29% of the total heat loss) were changed in either group.

However, it is important to note that during the fasting period the total heat losses were significantly higher in the control group (Table 3) and that they remained higher throughout the postprandial period.

Oxidation rate of the different substrates

The mean oxidation rates of the different substrates are shown in Fig. 1 and Table 4.

During the fasting period the control group oxidized mainly carbohydrate (90·4 mg/min) whereas the principal energy source utilized by the obese group was lipid (103·7 mg/min). The oxidation rates (mg/min) of the other substrates were: control group, 68·8 and 34·8 for lipid and protein respectively; obese group, 50·2 and 26·8 for carbohydrate and protein respectively.

After the glucose load, the oxidation rate of this substrate (carbohydrate) increased significantly in the control group; lipid utilization decreased slightly and protein metabolism remained virtually unchanged. Although there were similar over-all changes in substrate metabolism in the obese group, the fasting level for the oxidation rate of carbohydrate was approximately half that in the control group for the fasting period and, after the glucose load, the value for the oxidation rate of carbohydrate was similar to that in the control group for the fasting period.

Another point of interest is that the high level of utilization of lipid by the fasting obese subjects remained high after the glucose load.

Table 2. *Heat production (kJ/m² per h) obtained by indirect calorimetry (Ind) and heat losses (kJ/m² per h) measured by direct calorimetry (Dir) during a 40 min control period (fasting) and during five 30 min periods after a oral load of 50 g glucose*, for ten female control subjects and for eleven female obese subjects*

(Mean values with their standard errors)

Subject	Calorimetry	Period before glucose load (fasting)		Period after glucose load											
				1		2		3		4		5			
		Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean (% initial rate)†
								(*a*) Control subjects							
D	Ind	195·1	2·9	201·3	1·1	216·0	2·2	207·0	1·4	209·9	2·9	208·1	3·6	210·6	1·4	+ 7·9
M	Dir	226·1	5·1	226·1	5·1	213·6	4·0	224·9	2·5	218·4	4·4	230·7	3·8	222·7	3·0	− 1·5
C	Ind	149·4	5·8	169·2	2·2	172·1	4·3	175·0	5·0	165·2	1·8	166·7	4·3	170·0	1·8	+13·5
G	Dir	198·4	0·4	198·0	3·2	194·0	2·5	189·0	1·4	186·8	1·1	188·3	1·8	191·1	2·2	− 3·6
Bu	Ind	174·3	2·4	179·0	2·9	194·2	6·0	199·2	5·4	192·9	5·4	204·8	4·4	194·0	4·3	+11·3
F	Dir	174·5	1·1	174·5	1·1	179·5	2·4	184·0	1·0	183·9	1·9	176·3	0·7	179·6	1·9	+ 3·0
B	Ind	162·4	4·7	172·1	2·9	202·0	6·8	196·9	4·3	182·5	2·9	154·4	4·3	181·6	8·6	+11·8
S	Dir	165·7	1·1	165·7	1·1	165·7	1·1	168·4	1·4	168·4	1·4	159·1	1·4	165·5	1·7	− 0·1
D	Ind	189·3	3·4	214·8	6·4	220·5	6·1	228·3	4·4	214·0	4·6	208·0	4·8	217·2	3·4	+14·7
P	Dir	188·8	1·6	188·8	1·6	188·8	1·6	187·2	1·5	188·9	1·7	189·2	1·4	188·6	0·4	− 0·1
T	Ind	172·8	1·9	195·2	3·5	200·0	3·8	194·8	1·7	188·5	4·9	179·5	3·5	191·6	3·5	+10·9
D	Dir	182·0	0·7	181·5	0·7	181·5	0·7	181·5	0·7	183·5	0·7	185·4	0·4	182·3	0·8	+ 0·2
T	Ind	197·3	3·2	225·7	2·2	248·4	5·0	242·6	4·0	228·2	3·6	237·6	9·0	236·5	4·3	+19·9
M	Dir	205·9	0·9	200·0	1·0	190·7	1·2	200·7	0·9	193·3	1·2	191·7	1·2	195·3	2·1	− 5·1
Bo	Ind	190·5	4·4	203·8	12·5	202·6	4·2	208·7	2·4	205·9	3·4	204·8	3·1	205·2	1·0	+ 7·7
F	Dir	197·1	1·5	190·3	1·8	190·3	1·8	194·1	0·9	189·5	0·5	191·0	1·0	191·0	0·8	− 3·1
J	Ind	182·4	2·5	203·9	6·3	200·2	7·1	212·4	2·7	205·8	7·8	184·2	3·2	201·3	5·2	+10·4
G	Dir	193·8	2·5	193·0	1·7	193·0	1·7	196·4	0·9	198·1	1·4	193·0	2·1	194·7	1·1	+ 0·5
J	Ind	164·0	3·9	185·0	2·7	205·5	5·4	203·5	4·9	204·9	3·0	198·6	6·0	199·5	3·8	+21·6
C	Dir	187·6	1·3	185·1	1·3	187·0	0·9	187·0	1·2	191·0	1·4	192·9	1·0	188·6	1·4	+ 0·5
Mean	Ind	177·8	5·0	195·0	5·8	206·2	6·2	206·8	5·9	199·8	5·7	194·7	7·6	200·8	5·9	+13·0±1·5
	Dir	192·0	5·3	190·3	5·2	188·4	3·9	191·3	4·7	190·2	4·0	189·8	5·6	190·0	4·6	− 1·0±0·8

Table 2 *continued*

Subject	Calorimetry	Period before glucose load (fasting) Mean	SE	Period after glucose load: 1 Mean	SE	2 Mean	SE	3 Mean	SE	4 Mean	SE	5 Mean	SE	Mean	SE	Mean (% initial rate)†
								(*b*) Obese subjects								
Bs	Ind	145	2·9	150	1·1	148	1·8	147	1·4	—	—	—	—	148	0·7	+ 2·5
M	Dir	145	2·5	148	0·7	158	1·4	158	0·4	—	—	—	—	155	3·2	+ 6·4
F	Ind	180	2·9	214	8·6	210	5·4	201	6·5	181	3·6	—	—	201	6·8	+11·8
M	Dir	187	7·6	180	6·5	184	2·2	186	2·5	172	1·1	—	—	181	3·2	− 3·5
DA	Ind	165	4·7	181	3·2	177	1·1	170	1·4	168	4·0	162	5·4	171	3·2	+ 3·9
L	Dir	154	3·2	133	2·9	142	2·5	147	1·1	153	2·9	148	1·4	144	4·3	− 6·8
S	Ind	186	1·8	212	4·3	207	4·0	197	4·3	194	6·5	195	3·2	201	3·6	+ 8·1
B	Dir	160	2·2	175	2·9	174	3·2	175	2·5	178	3·2	181	5·8	176	1·4	+10·1
SA	Ind	158	2·5	181	1·4	175	4·7	169	1·4	179	2·9	174	3·2	176	2·2	+11·4
M	Dir	184	1·1	184	6·8	185	5·4	175	5·4	166	4·0	161	3·2	174	4·7	− 5·5
H	Ind	166	6·1	177	2·2	186	4·3	175	6·5	169	5·0	169	4·0	175	3·2	+ 5·6
M	Dir	166	1·8	166	1·8	166	1·8	164	2·5	156	1·8	157	2·2	162	2·2	− 2·6
GJ	Ind	144	1·1	140	1·8	148	1·4	143	1·1	142	2·5	147	3·2	144	1·4	0
M	Dir	153	0·7	162	4·0	159	1·1	162	1·1	161	2·2	154	1·4	160	1·4	+ 4·0
S	Ind	167	16·6	163	5·0	161	10·4	164	3·2	162	6·1	166	5·8	163	0·7	− 2·2
T	Dir	156	3·2	159	1·8	163	2·9	167	2·9	171	2·5	152	2·5	162	3·2	+ 4·2
L	Ind	157	1·4	171	2·2	163	2·5	166	3·6	169	2·5	165	2·5	167	1·4	+ 6·2
B	Dir	167	3·2	167	3·2	161	1·1	162	0·7	167	2·5	162	2·2	164	1·4	− 1·7
G	Ind	148	2·9	166	2·5	160	4·3	150	1·8	152	2·5	154	3·6	156	2·9	+ 5·6
C	Dir	152	2·5	147	2·9	143	2·2	145	1·8	139	1·4	136	5·8	142	2·2	− 7·6
P	Ind	189	1·8	200	1·4	200	3·2	196	2·9	195	4·3	193	1·8	197	1·4	+ 3·8
M	Dir	164	1·1	159	1·1	160	1·8	157	1·4	161	2·5	163	2·9	160	1·1	− 2·2
Mean	Ind	164	4·8	178	7·1	176	6·8	171	6·1	171	5·4	169	5·3	173	6·1	+ 5·2 ± 1·3
	Dir	163	4·0	162	4·5	163	4·3	163	3·7	162	3·6	157	4·1	162	3·7	− 0·5 ± 1·7

* For details of experimental procedures, see p. 282.

† Mean increase in metabolic rate during 150 min after glucose load as a percentage of the fasting metabolic rate (before glucose load).

Table 3. *Comparison of the metabolic rates and of the total heat losses, before and after an oral load of 50 g glucose, for a group of ten female control subjects and for a group of eleven female obese subjects*†

(Mean values with their standard errors)

	Period of measurement	Control		Obese	
		Mean	SE	Mean	SE
Metabolic rate (kJ/m² per h)	B	177·8	5·0	164·1	4·8^{NS}
	A	200·8	5·9	172·6	6·1**
Total heat losses (kJ/m² per h)	B	192·0	5·3	162·6	3·9***
	A	189·9	4·6	161·8	3·7***
Change in metabolic rate (% initial rate)‡		+13·0	1·5	+5·2	1·3***
Change in total heat losses (% initial rate)‡		−1·0	1·5	−0·5	1·7^{NS}

^{NS}, not significant; B, before glucose load (fasting period); A, during 150 min after glucose load. Differences between mean values for the two groups were statistically significant (unpaired *t* test): ** $P<0.005$; *** $P<0.001$.

† For details of subjects, see Table 1, and for details of experimental procedures, see p. 282.

‡ Mean change during 150 min after glucose load as a percentage of the fasting value (before glucose load).

Temperatures

The values for the internal and skin temperatures are given in Table 5. After the glucose load, the internal temperature of the control subjects tended to increase (+0·18°), whereas the mean skin temperature remained unchanged.

In the obese subjects, the glucose load did not cause any significant increase in either the internal or the skin temperature.

The results given in Table 5 indicate that the internal temperature of the control subjects was significantly higher than that of the obese subjects during the postprandial period. Furthermore, the mean skin temperature of the control group was significantly higher than that of the obese group and remained higher throughout the postprandial period.

Thermal balance

All control subjects were in negative thermal balance (heat production minus heat losses) during the fasting period ($-14{\cdot}2 \pm 5{\cdot}0$ kJ/m² per h), i.e. their heat losses were greater than their heat production (Fig. 2). After the glucose load the amount of heat stored increased significantly and the thermal balance became positive ($+10{\cdot}8 \pm 5{\cdot}6$ kJ/m² per h). However, the obese subjects were already in slight positive balance in the preprandial state ($+1{\cdot}4 \pm 4{\cdot}8$ kJ/m² per h). This positive balance was further reinforced after the glucose load ($+10{\cdot}8 \pm 4{\cdot}8$ kJ/m² per h).

Energy-free meal

The possibility that the effects we have found were caused by the glucose carrier were minimal. However, three control experiments were done using three of the lean control subjects to study the effect of an oral load of the same volume but without glucose, i.e. 150 ml water + lemon juice. No significant changes in metabolic rate or

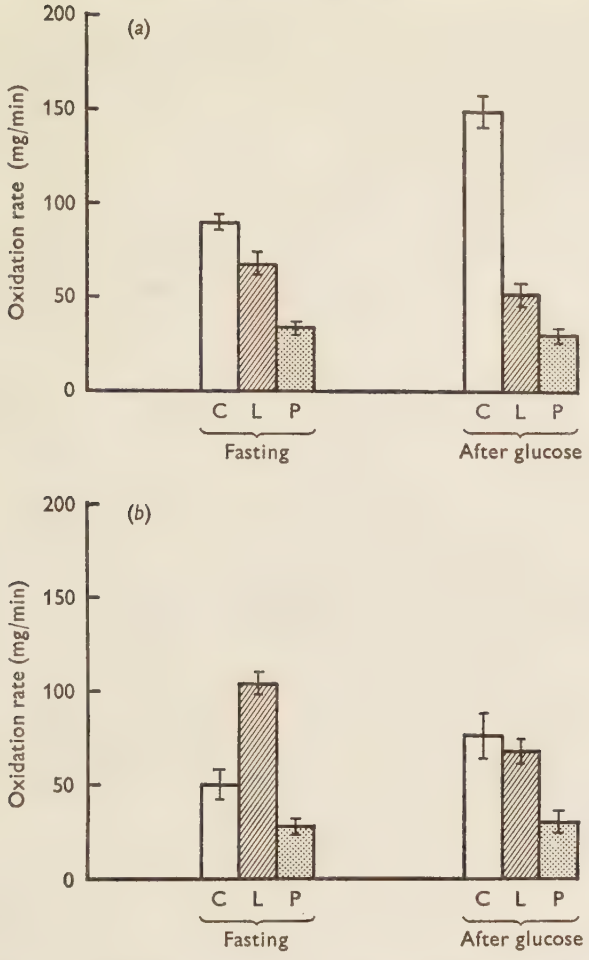

Fig. 1. Mean oxidation rates (mg/min) of different substrates (C, carbohydrates; L, lipids; P, proteins) during a 40 min control period (fasting) and during 150 min after an oral dose of 50 g glucose, for (*a*) group of ten female control subjects and for (*b*) group of eleven female obese subjects. The increase in the glucose oxidation rate after the glucose load was statistically significant for both groups: $P < 0{\cdot}001$. Vertical bars represent the standard errors of the mean values.

total heat losses were found (Table 6). The negative thermal balance obtained in the fasting period persisted throughout the experiment. Mean skin temperature was not modified but the internal temperature decreased significantly during the experiment (Table 7) confirming the negative thermal balance. The fasting oxidation rates of the substrates were similar to those obtained in the first part of this experiment and were not significantly modified after ingestion of the energy-free meal (Table 7).

On the basis of these results, we can conclude that an energy-free meal of 150 ml water + lemon juice had no significant effect on metabolic rate. Therefore the findings reported in the first part of this study were due to the glucose load.

Table 4. *Mean oxidation rate (mg/min) of carbohydrate, fatty acids (lipid) and amino acids (protein), obtained by indirect calorimetry and from urinary nitrogen measurements before and after an oral load of 50 g glucose, for a group of ten female control subjects and for a group of eleven female obese subjects*‡

(Mean values with their standard errors)

		Metabolites oxidized					
		Carbohydrate		Fatty acids		Amino acids	
Subjects	Period of measurement	Mean	SE	Mean	SE	Mean	SE
Control	B	90·4	3·4	68·8	6·1	34·8	3·0
	A	159·1	8·6***	51·8	5·5**	29·6	3·9^{NS}
		†††		†††		NS	
Obese	B	50·2	7·5	103·7	6·0	26·8	4·4
	A	95·6	11·8***	88·6	7·0*	30·0	5·9^{NS}

NS, not significant; B, before glucose load (fasting period); A, during 150 min after glucose load.

Changes in mean oxidation rates for each metabolite for period A were statistically significant: * $P<0·01$; ** $P<0·005$; *** $P<0·001$.

Differences between mean values for oxidation rates for the two groups for period B and for period A were statistically significant (unpaired t test): ††† $P<0·001$.

‡ For details of subjects, see Table 1, and for details of experimental procedures, see p. 282.

Table 5. *Internal temperature* (T_{int}) (°) *and mean skin temperature* (T_{cut}) (°) *measured during the 40 min control period (fasting) (initial* T) *and during the final 10 min (final* T) *of the 150 min period after an oral dose of 50 g glucose, for a group of ten female control subjects and for a group of eleven female obese subjects*†

(Mean values with their standard errors)

		Initial T		Final T		Change in T	
		Mean	SE	Mean	SE	Mean	SE
Control	T_{int}	36·80	0·10	36·98	0·10	0·18	0·05
		NS		**			
Obese	T_{int}	36·71	0·05	36·72	0·04	0·01	0·04
Control	T_{cut}	33·72	0·08	33·72	0·09	0·00	0·02
		**		*			
Obese	T_{cut}	33·29	0·11	33·41	0·11	0·12	0·05

The change in T for T_{int} and for T_{cut} for both groups was not statistically significant (paired t test). NS, not significant.

Differences between mean values for T_{int} and for T_{cut} for the two groups were statistically significant (unpaired t test): * $P<0·05$; ** $P<0·02$.

† For details of subjects, see Table 1, and for details of experimental procedures, see p. 282.

DISCUSSION

Obesity is not always the consequence of an absolute excess of energy intake; this excess can be relative if it is accompanied by a decreased energy expenditure. The main factors contributing to decreased energy expenditure in obese subjects are (*a*) decreased physical activity, (*b*) increased energy efficiency of the utilization of nutrients or (*c*) a lack of thermogenic stimulation, or both *b* and *c*.

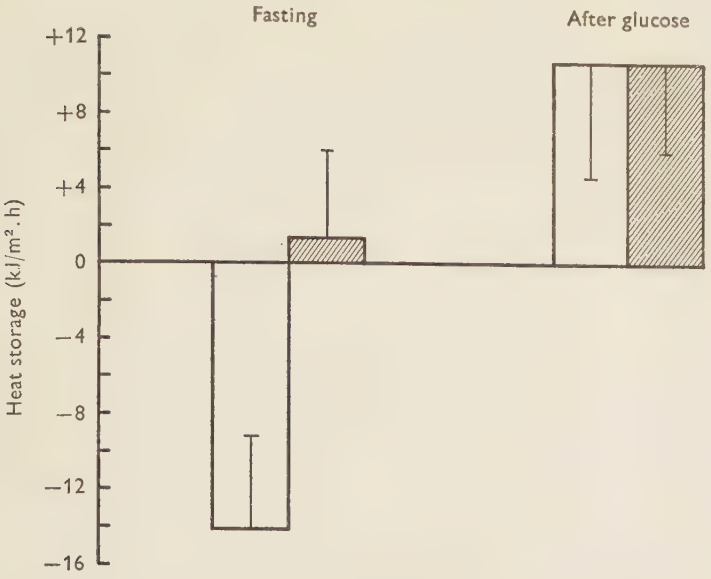

Fig. 2. Mean thermal balance (heat storage (kJ/m² per h), i.e. heat production minus heat losses) during a 40 min control period (fasting) and during 150 min after an oral dose of 50 g glucose, for a group of ten female control subjects (□) and for a group of eleven female obese subjects (▨). The change in thermal balance after the glucose load was statistically significant: for control group, $P<0{\cdot}001$; for obese group, $P<0{\cdot}05$. Vertical bars represent the standard errors of the mean values.

It is not the aim of this paper to discuss factors *a* and *b* extensively. Decreased physical activity in the obese individual has often been described. Björntorp (1966) has found that lipogenesis from glucose is twice as high in the obese as in 'normal-weight' subjects. There are a few biochemical pathways in intermediary metabolism which can modify energy efficiency, i.e. synthesis of fatty acids from glucose, and oxidation of the glucose produced (Ball & Jungas, 1964), the esterification–hydrolysis cycle for fatty acids (Ball, 1965), and the glycerophosphate–dihydroxyacetone cycle (Galton & Bray, 1967).

Lack of thermogenic stimulation in the obese individual can be accounted for by a weak, dietary-induced thermic effect, and by a low metabolic response to cold.

The results of this study indicate that at an ambient temperature of 28°, obese subjects have smaller heat losses than control subjects. These results are in agreement with those of Gygax, Pittet & Jéquier (1972) and Jéquier, Gygax, Pittet & Vannotti (1974), who reported similar findings at ambient temperatures of 28 and 20°; after 2 h exposure at 20°, the control subjects tended to stimulate their metabolic rate, but the obese subjects did not.

Our results indicate that, although both obese and control subjects stimulate their metabolic heat production after an oral load of 50 g glucose, this thermic effect was lower in the obese group (only half that of the control group).

The fasting oxidation rates of the different substrates were different in the obese subjects when compared with the control subjects. The latter oxidized more carbo-

Table 6. *Heat production (kJ/m² per h) obtained by indirect calorimetry (Ind) and heat losses (kJ/m² per h) measured by direct calorimetry (Dir) during a 40 min control period (fasting) and during five 30 min periods after the ingestion of an energy-free meal (150 ml water + lemon juice), for three female control subjects**

(Mean values with their standard errors)

Subjects	Calorimetry	Period before energy-free meal (fasting)		Period after energy-free meal											
				1		2		3		4		5			
		Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean (% initial rate)†
J	Ind	173·8	0·6	175·6	3·8	171·7	2·0	178·4	2·8	180·3	4·4	180·8	4·5	177·4	1·7	+ 2·1
D	Dir	179·9	0·8	179·9	0·8	178·4	0·7	180·6	1·0	176·4	0·8	175·6	1·6	178·1	0·9	− 1·0
Bo	Ind	169·5	2·3	171·5	3·8	168·4	4·6	172·7	7·1	176·8	2·6	172·7	4·4	172·4	1·3	+ 1·7
F	Dir	173·4	2·0	174·1	2·1	174·1	1·0	182·0	0·9	177·3	0·5	182·8	2·0	178·1	1·7	+ 2·7
Bu	Ind	156·2	8·1	156·5	8·9	151·5	2·3	156·4	5·0	155·2	3·2	153·7	3·7	154·7	0·9	− 1·0
F	Dir	177·7	2·0	176·7	2·5	175·1	1·7	179·2	0·9	178·5	1·1	176·9	0·8	177·3	0·7	− 0·2
Mean	Ind	166·5	5·3	167·9	5·8	163·9	6·3	169·2	6·6	170·8	7·8	169·1	8·0	168·2	6·9	+ 1·0
	Dir	177·0	1·9	176·9	1·7	175·9	1·3	180·6	0·8	177·4	0·6	178·4	2·2	177·8	0·3	+ 0·5
Thermal balance‡		−10·5	5·5											−9·7	6·6	

* For details of experimental procedures, see p. 282.

† Mean increase in metabolic rate during 150 min after energy-free meal, as a percentage of the fasting metabolic rate (before energy-free meal).

‡ The difference between heat production and heat losses.

Table 7. *Internal temperature* (T_{int}) (°) *and mean skin temperature* (T_{cut}) (°) *measured during the* 40 *min control period (fasting) and during the final* 10 *min of the* 150 *min period after the ingestion of an energy-free meal* (150 *ml water + lemon juice*), *and mean oxidation rate (mg/min) of carbohydrate, fatty acids (lipid) and amino acids (protein) obtained by indirect calorimetry and from urinary nitrogen measurements before and after the meal, for three female control subjects*†

(Mean values with their standard errors)

	Period of measurement					
	Before meal		After meal		Change in T	
	Mean	SE	Mean	SE	Mean	SE
T_{int}	36·71	0·03	36·58	0·02	−0·13	0·02*
T_{cut}	33·35	0·16	33·40	0·15	+0·05	$0·01^{NS}$
Mean oxidation rates:						
Carbohydrate	95·7	3·4	93·6	$8·3^{NS}$		
Fatty acids	76·4	12·1	83·8	$10·7^{NS}$		
Amino acids	46·8	2·2	31·0	$3·8^{NS}$		

Changes in mean oxidation rates for each metabolite after the energy-free meal were not statistically significant.

NS, not significant.

The change in T for T_{int} was statistically significant: * $P<0·01$.

† For details of experimental procedures, see p. 282.

hydrate (90·4 mg/min) than lipid (68·8 mg/min), whereas the fasting obese subjects oxidized more lipid (103·7 mg/min) than carbohydrate (50·2 mg/min). After the glucose load there was an increase in glucose metabolism in both groups, but it was much lower in the obese than in the control subjects.

Felber, Moody & Vannotti (1965) reported a decrease in the glucose tolerance of non-obese subjects when the concentration of circulating free fatty acids is increased by an infusion of lipids preceding the glucose load. Gomez *et al.* (1972) suggested that this glucose intolerance was probably due to inhibition of carbohydrate oxidation rate by metabolites of free fatty acids as described by Randle, Hales, Garland & Newsholme (1963) in muscle tissue. A similar mechanism could account for our results in obese subjects.

In our ambient conditions, the thermal balance obtained indicated that the two groups were in a different starting state. The fasting control subjects were in negative thermal balance, their heat losses were greater than their metabolic heat production and their temperatures tended to decrease. On the other hand, fasting obese subjects were in thermal balance, their metabolic heat production was slightly higher than their heat losses and their body temperature was stable.

The ingestion of the glucose induced an important modification in the thermic state of the control subjects: from a negative level, i.e. from a deficit of heat, they reached a positive thermal balance.

In the obese subjects, ingestion of the glucose did not cause such an important

change in their thermic state. Glucose ingestion only induced a reinforcement of a pre-existing, equilibrated thermal balance.

Thus, the results of this study suggest that an inefficient stimulation of thermogenesis might be a factor contributing to the low energy expenditure of the obese individual. This decreased dietary-induced thermic effect may be due in part to inhibition of glucose oxidation by fatty acid metabolites.

It remains to be determined whether the equilibrated thermal balance of the obese individual is involved in inhibiting the thermic effect found after glucose ingestion. The thermic effect of protein and lipid should also be carefully studied in the obese individual.

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Thermic effect of glucose and amino acids in man studied by direct and indirect calorimetry

By PH. PITTET, P. H. GYGAX AND E. JÉQUIER

Department of Clinical Physiology and Institute of Physiology, University of Lausanne, 1011 *Lausanne, Switzerland*

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1. In order to reinvestigate the classical concept of specific dynamic action of food, the thermic effect of ingested glucose (50 g) or essential amino acids (50 g) or both was measured in seven healthy male subjects dressed in shorts, by using both direct and indirect calorimetry simultaneously. Experiments were performed under conditions of thermal comfort at 28°.

2. Energy 'balance' (heat production minus heat losses) was negative during the control period (mean heat deficit: $-16{\cdot}0 \pm 0{\cdot}8$ kJ/m² per h.

3. Metabolic rate increased $13{\cdot}6 \pm 1{\cdot}8$% after the glucose load, $17{\cdot}2 \pm 1{\cdot}4$% after amino acids, and $17{\cdot}3 \pm 2{\cdot}9$% after both glucose and amino acids: thus there was no additive thermic effect when both nutrients were given together.

4. In contrast to the metabolic rate, heat losses were not significantly altered after nutrient ingestion; consequently, the energy 'balance' became rapidly positive.

5. These results show that: (*a*) the food-induced thermogenesis, for a moderate energy intake, is less dependent on the nature of the nutrients than was classically admitted; (*b*) this increased heat production mainly induces changes in heat storage rather than in heat losses during the first hours following ingestion of a meal.

An increased heat production following food ingestion was described by Rubner (1902) at the beginning of the century. Lusk (1930) showed that the stimulation of heat production varied according to the composition of the diet. Proteins had the greatest effect, increasing the metabolic rate by 30% of the ingested energy, whereas the augmentation was 6 and 4% for lipids and carbohydrates respectively. The term 'specific dynamic action' was used to describe this effect. It is to be emphasized that most of these early experiments were performed on animals given large amounts of nutrients.

The concept of specific dynamic action (SDA) has been recently challenged by various authors (Miller & Mumford, 1967; Ashworth, 1969; Garrow & Hawes, 1972; Garrow, 1973; Miller & Mumford, 1973). According to Miller & Mumford (1973), the term 'thermic effect' appears more appropriate to account for the increased metabolic rate following food ingestion.

Since precise quantitative findings on the thermic effect of food in human subjects are scarce in the literature, the present study was undertaken to measure the energy balance of subjects receiving glucose or amino acids or both. For this purpose, determinations of metabolic rate were made simultaneously with measurements of heat losses in a direct calorimeter.

EXPERIMENTAL

Seven healthy male students were studied. The physical characteristics of the subjects are summarized in Table 1.

Table 1. *Main physical characteristics of the seven male human subjects*

Subject	Age (years)	Height (m)	Body surface (m^2)	Wt (kg)	Percentage of ideal wt (%)
G.N.	22	1·82	1·95	74·7	108
B.D.	19	1·76	1·75	61·0	94
C.J.	20	1·90	2·05	77·7	103
G.P.	25	1·77	1·81	65·4	100
M.M.	23	1·73	1·77	64·0	102
H.M.	20	1·70	1·89	77·9	129
S.J.-Cl.	21	1·82	2·02	81·1	117
Mean	21·4	1·79	1·89	71·7	107·6
SE	0·8	0·03	0·05	3·0	4·5

The seven subjects were given the three following meals: (1) ingestion of 50 g glucose; (2) ingestion of 50 g of a balanced mixture of essential amino acids (Nesmida; Nestlé Company, Vevey, Switzerland); (3) ingestion of 50 g glucose + 50 g of the mixture of amino acids. One subject (G.N.) did not perform the third test.

Subjects were fasted for 12 h before the experiment. After a period of rest of 1 h in a constant-temperature room (at 28° and 30% relative humidity), the fasting subject, dressed in shorts, was introduced into the calorimeter; the ambient conditions in the calorimeter were identical to those of the constant-temperature room. Control measurements were taken during 40 min; then the subject received the test meal and measurements were taken during a period of 2·5 h. The following measurements were made continuously during the tests: internal temperature, by a tympanic probe and a sublingual probe; mean skin temperature, by weighting eight different skin temperatures according to Hardy & Du Bois (1937); metabolic rate and respiratory quotient (RQ) from determinations of ventilation and of the concentration of O_2 and CO_2 in the expired air in an open circuit (Gomez, Jéquier, Chabot, Büber & Felber, 1972).

The amount of protein (or amino acids) metabolized was calculated from the urinary nitrogen excretion (Du Bois, 1924). The non-protein respiratory quotient was then determined, and the tables of Lusk (1924) were used for computing the amounts of carbohydrates and lipids which were oxidized during the test.

The total heat losses were measured by gradient layer direct calorimetry (Spinnler, Jéquier, Favre, Dolivo & Vannotti, 1973); this method enables separate measurements of 'dry heat losses' (radiation + convection) and evaporative heat losses (insensible perspiration and sweating), to be carried out.

Statistical analyses were performed with Student's t test for paired or unpaired results. The threshold of significance was chosen for a $P < 0{\cdot}05$.

RESULTS

After the three test meals, the metabolic rate measured over a period of 150 min increased significantly, by 13·6% of the initial rate for glucose, by 17·2% for amino acids and by 17·3% for the meal of glucose + amino acids (Fig. 1 and Table 2). The increments observed in the three tests (ΔM) are not significantly different.

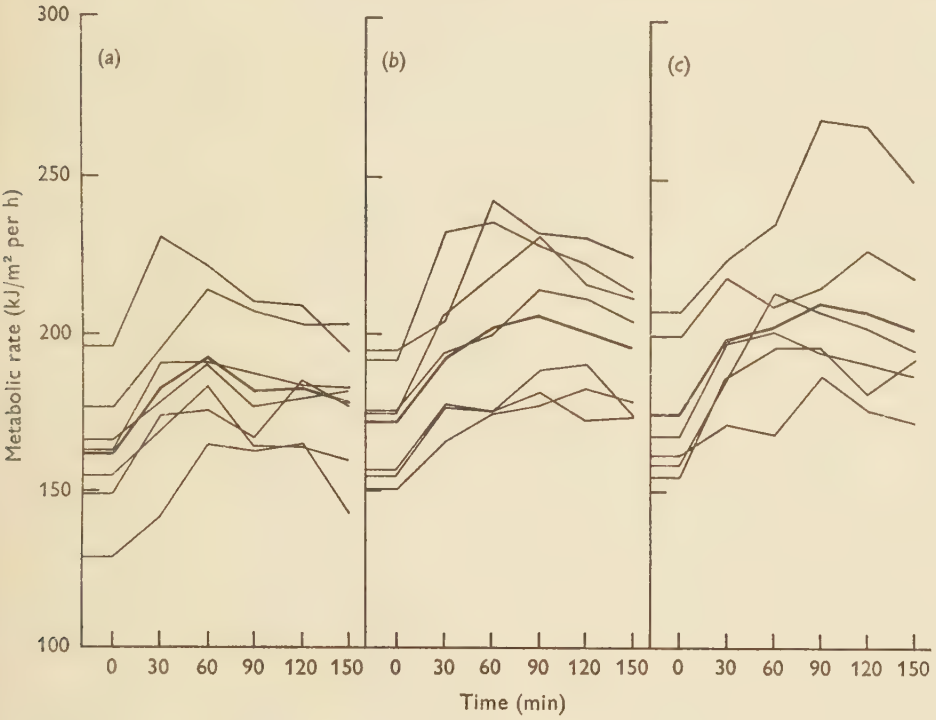

Fig. 1. Metabolic rate of male human subjects during a 40 min control period and during five periods of 30 min after ingestion of: (*a*) 50 g glucose, (*b*) 50 g amino acids and (*c*) 50 g glucose + 50 g amino acids. The thick line represents the mean value for the group. The mean increase in metabolic rate for each meal is given in Table 2. The degree of significance of the variation of the metabolic rate after each meal was: (*a*) $P < 0{\cdot}001$, (*b*) $P < 0{\cdot}001$, (*c*) $P < 0{\cdot}01$. Paired *t* tests on the increase in metabolic rate between the three loads showed no significant differences between them.
Time 0: mean value for the 40 min control period.

It is important to note that we obtained an increase of metabolic rate with the single load of 840 kJ (200 kcal) supplied either as glucose or amino acids similar to the stimulation observed after the double nutrient load (1680 kJ or 400 kcal).

Catabolism of the different substrates is shown in Table 3. After the ingestion of glucose, the oxidation rate of this substrate increased, whereas the catabolism of lipid and protein was about unchanged. After the ingestion of amino acids, the catabolism of these nutrients alone was increased. The combined meal induced an increase in glucose oxidation similar to that in the first test, whereas amino acid consumption was lower than in the second test.

Table 2 shows the metabolic rate and the total heat losses before and after the test meal. During the period following the meal, the total heat losses were not modified; similarly, the insensible perspiration, which represented 27 % of the total heat losses, was unaffected by the meal.

The thermal energy 'balance' (gains or losses in heat) can be determined by calculation of the difference between metabolic rate and heat losses. In all subjects, the energy balance was negative during the control period: their heat losses were larger than their

Table 2. *Heat production, in male human subjects, calculated by indirect calorimetry (ind) and heat losses measured by direct calorimetry (dir) in a 40 min control period and during five 30 min periods after the ingestion of a meal of (a) glucose (50 g) (b) essential amino acids (50 g) or (c) both (kJ/m² per h,* ± SE)

Subject	calorimetry	Before (control)	After (30 min periods) 1	2	3	4	5	Mean	Mean as % of controls*
			(*a*) Glucose meal						
B.D.	Ind	149±3·3	174±1·7	176±0·7	166±2·0	185±3·3	177±4·0	176±3·1	+18·1
	Dir	155±1·0	161±1·4	160±0·5	145±1·6	159±5·4	173±3·4	160±4·1	+3·2
S.J.	Ind	166±2·0	180±0·6	190±5·1	177±3·2	179±5·0	183±2·7	182±2·2	+9·6
	Dir	187±0·2	178±0·9	186±2·4	185±2·1	177±1·1	175±0·7	181±2·1	−3·2
C.J.	Ind	177±1·4	196±7·3	214±4·6	207±2·6	203±1·1	203±1·8	205±3·0	+15·8
	Dir	180±7·2	192±1·6	206±8·5	211±2·6	206±4·3	205±1·8	204±3·2	+13·3
G.P.	Ind	163±0·6	191±3·6	191±5·5	186±3·1	184±2·4	183±1·4	187±1·8	+14·7
	Dir	195±1·5	189±1·7	186±1·3	186±0·8	185±0·1	185±0·7	186±0·7	−4·6
M.M.	Ind	129±4·9	142±6·8	165±2·2	163±3·7	165±0·6	143±3·1	155±5·4	+20·2
	Dir	171±4·2	177±0·2	185±1·7	186±2·8	181±1·4	179±3·1	182±1·8	+6·4
H.M.	Ind	155±9·1	169±6·9	183±0·6	163±1·5	165±2·6	160±3·1	168±4·1	+8·4
	Dir	210±5·0	175±0·9	182±0·7	183±1·0	183±0·7	184±0·4	181±1·7	−13·8
G.N.	Ind	196±2·2	231±3·5	222±8·6	210±1·2	209±2·7	194±3·6	213±6·2	+8·7
	Dir	185±2·9	191±1·7	194±3·5	193±1·2	192±0·9	185±3·2	191±1·7	+3·2
Mean	Ind	162±7·2	183±10·4	192±7·6	182±7·6	184±6·5	178±7·8	184±7·6	+13·6± 1·8
	Dir	183±6·6	180±4·2	186±5·3	185±7·3	184±5·3	185±4·0	184±5·1	+0·6± 3·3
			(*b*) Amino acid meal						
B.D.	Ind	157±1·8	177±2·5	176±2·3	182±1·9	173±4·4	174±3·2	176±1·5	+12·1
	Dir	153±2·6	159±2·5	150±0·7	169±3·2	177±2·2	164±1·7	164±4·5	+7·2
S.J.	Ind	175±1·0	194±3·3	200±5·0	215±3·6	202±3·7	195±1·0	201±3·6	+14·9
	Dir	197±7·9	183±1·1	178±0·8	183±1·6	185±2·1	181±0·4	182±1·2	−7·6
C.J.	Ind	195±5·9	204±4·7	243±5·0	232±8·1	231±3·6	225±1·6	227±6·5	+16·4
	Dir	205±0·5	189±3·6	207±3·1	213±6·7	221±0·6	225±0·4	211±6·4	+2·9
G.P.	Ind	155±3·1	178±3·2	176±5·5	189±2·8	191±1·9	185±5·6	184±3·0	+18·7
	Dir	214±0·7	205±1·9	198±1·9	203±1·2	203±1·1	208±4·3	203±1·6	−5·1
M.M.	Ind	193±2·1	233±9·0	236±2·9	229±7·6	223±4·4	214±2·0	227±3·9	+17·6
	Dir	213±2·1	203±1·0	197±2·1	195±2·1	194±2·3	192±1·8	197±1·9	−7·5
H.M.	Ind	151±0·5	166±2·4	175±1·9	178±2·7	183±3·0	179±0·7	176±2·7	+16·6
	Dir	175±1·3	186±3·2	184±1·6	196±2·8	202±0·1	201±0·5	194±3·7	+10·9
G.N.	Ind	175±1·8	205±0·1	219±1·4	231±1·0	216±5·5	212±4·0	217±4·3	+24·0
	Dir	161±1·9	177±2·7	178±2·3	184±3·6	192±3·2	202±0·4	186±4·7	+15·5
Mean	Ind	172±6·9	194±8·5	204±11·3	208±9·2	203±8·4	198±7·6	201±8·9	+17·2± 1·4
	Dir	188±9·6	186±5·6	185±7·1	192±5·5	196±5·3	196±7·4	191±5·8	+2·3± 3·6

Table 2. (*cont.*)

(*c*) Glucose + amino acid meal

Subject	calorimetry	Before (control)	After (30 min periods) 1	2	3	4	5	Mean	Mean as % of controls*
B.D.	Ind	160±2·5	185±2·6	214±9·2	208±3·5	203±2·6	196±1·8	201±5·0	+25·6
	Dir	176±0·2	183±0·3	183±3·4	181±1·9	192±2·5	185±1·8	185±1·9	+5·1
S.J.	Ind	200±0·7	223±3·7	204±5·1	210±8·9	233±0·7	224±5·4	219±5·1	+9·5
	Dir	195±3·2	182±1·4	180±1·0	174±0·8	170±0·7	172±2·7	176±2·3	−9·7
C.J.	Ind	207±0·5	226±1·9	236±5·9	270±9·4	268±6·0	250±9·1	250±8·7	+20·8
	Dir	192±2·4	195±3·3	190±3·1	214±7·8	223±1·9	221±0·9	209±6·8	+8·9
G.P.	Ind	168±1·8	198±1·5	202±1·9	195±0·9	192±4·0	188±0·5	195±2·4	+16·1
	Dir	193±3·9	187±0·8	189±1·7	190±3·3	193±2·4	189±4·7	190±1·0	−1·6
M.M.	Ind	155±1·0	186±2·4	196±1·0	197±4·5	182±4·6	194±0·7	191±3·0	+23·2
	Dir	180±1·2	177±0·3	182±2·0	187±1·5	186±3·4	195±0·7	185±2·9	+2·8
H.M.	Ind	162±0·8	172±2·8	169±3·1	187±4·3	177±4·3	173±3·2	176±3·0	+8·6
	Dir	183±1·7	185±3·0	188±5·8	195±1·9	201±1·1	199±3·0	194±3·0	+6·0
Mean	Ind	175±9·1	198±8·0	203±8·9	211±12·3	209±14·0	204±11·4	205±10·0	+17·3±2·9
	Dir	186±6·7	185±2·4	185±1·7	190±5·7	194±7·2	194±6·6	190±4·5	+1·9±2·7

* Indicates the mean increase in metabolic rate during 150 min given as a percentage of the initial metabolic rate.

Table 3. *Mean oxidation rate* (*mg/min*), *in male human subjects, of carbohydrates, fatty acids and amino acids calculated by indirect calorimetry and by urinary nitrogen measurements before and after test meals of glucose* (50 *g*), *essential amino acids* (50 *g*) *or both*

Test meal		Metabolites oxidized: Carbohydrates Mean	SE	Fatty acids Mean	SE	Amino acids Mean	SE
Glucose	Before	108·0	20·7	69·6	7·7	26·8	3·1
	After	173·7	13·8***	58·4	7·1*	26·4	2·7*
Amino acids	Before	134·5	29·7	61·2	6·3	24·8	2·4
	After	145·7	30·0*	70·5	12·1*	41·8	5·5**
Glucose + Amino acids†	Before	124·2	23·0	79·2	12·0	24·9	3·7
	After	187·0	37·5**	63·3	11·3*	36·6	4·8**

† Six subjects only. * Difference not significant.
** Significant difference. $P < 0·05$. *** Significant difference, $P < 0·001$.

heat production. This heat deficit (general mean of $-16·0 \pm 0·8$ kJ/m² per h) is changed into either a heat equilibrium or a slightly positive energy balance after ingestion of the meal. In these conditions, one can observe a trend towards increasing body temperatures, mainly internal temperature (Table 4).

DISCUSSION

This study shows that the thermic effect of food can be demonstrated even with a low amount of ingested energy, whereas most previous studies were performed with greater energy intake (Rubner, 1902; Benedict & Carpenter, 1918; Lusk, 1930; Strang & McCluggage, 1931).

Table 4. *Initial and final temperature (T), internal (int) and cutaneous (cut), of male human subjects measured at 5 min and 145 min respectively after ingestion of a meal*

Test meal		Initial T (°C)	Final T (°C)	ΔT	Paired t test
Glucose	T int	36·59 ± 0·13	36·72 ± 0·08	0·13 ± 0·04	NS
	T cut	33·82 ± 0·11	33·95 ± 0·10	0·13 ± 0·05	NS
Amino acids	T int	33·66 ± 0·10	36·88 ± 0·10	0·22 ± 0·09	NS
	T cut	33·83 ± 0·09	33·94 ± 0·11	0·11 ± 0·07	NS
Glucose + amino acids	T int	36·56 ± 0·10	36·82 ± 0·09	0·26 ± 0·04	$P < 0·01$
	T cut	33·68 ± 0·10	33·83 ± 0·13	0·15 ± 0·05	$P < 0·02$
Mean	T int	36·62 ± 0·06	36·81 ± 0·05	0·19 ± 0·05	$P < 0·01$
	T cut	33·78 ± 0·06	33·91 ± 0·08	0·13 ± 0·05	$P < 0·02$

NS, non-significant.

Since the thermic effect of amino acids lasts longer than that of glucose, a small part of the total effect has not been measured within the test period. However, this appears to be a small cause of error, since most measurements of metabolic rate were on the way to reaching their initial value towards the end of the test. In all individual cases, the value for the last 30 min period is equal to, or more frequently lower than, the mean value for the test period.

We have recalculated our results according to the classical concept for SDA. With a 840 kJ (200 kcal) oral load of glucose, a specific effect of 4 % corresponds to a metabolic increase of 33·5 kJ. In our study, we found 101·9 kJ, or a SDA of 12·1 %. With the 840 kJ amino acid loads, the classically predicted extra metabolism should be 30 % of this ingested energy, or 252 kJ. We found 139 kJ for the test period, or a SDA of 16·5 %. According to Forbes, when glucose and proteins are combined, the dynamic effect is 12·5 % less than that predicted from the sum of their individual effects (Ganong, 1969): therefore, with the glucose + amino acid load (1680 kJ), the extra metabolism should be 29·7 %, or 498 kJ. In this study, we found 142 kJ only, or a SDA of 8·5 %. These results illustrate the protein-sparing effect of carbohydrates in man.

Our results show that, during the test period, the increase in energy expenditure was little affected by the nature or even by the amount of the nutrients and therefore is quite different from that described in the classical concept of SDA.

Our results are in agreement with those of Gomez *et al.* (1972), who observed in human subjects a mean increase in metabolic rate of 11 % during the 3 h following a 1680 kJ (400 kcal) oral glucose load, and with a recent study of Garrow (1973), who studied the thermic effect of three meals with a larger energy content of 2720 kJ (650 kcal). This author observed an increase by 12 % of the metabolic rate with a glucose meal, by 17 % with gelatin, and by 15 % with milk proteins + glucose.

The larger thermic effect of proteins reported in the early literature might be simply explained by the fact that restrained animals (dogs) felt livelier and were more active when they received a large amount of meat than when they got an equivalent amount of energy as carbohydrates.

For a moderate energy intake (840 kJ and 1680 kJ in the present study, and 2720 kJ in Garrow's (1973) study), the thermic effect appears to be relatively independent of the meal size. However, with larger meals, especially in chronically overfed subjects, Miller, Mumford & Stock (1967) described a 'diet-induced thermogenesis' which was related to the meal size. However, in this latter study, the subjects received a large energy intake during a prolonged period (2–3 weeks). Under these conditions, a metabolic adaptation of energy expenditure to its intake occurs.

In conclusion, our results show that the dynamic action of nutrients is less specific than was classically admitted. Moreover, in the range of energy intake studied, the thermic effect of nutrients is not dependent on the total amount of energy given.

Finally, the increased heat production by 'diet-induced thermogenesis' mainly induces changes in heat storage rather than in heat losses during the first hours following ingestion of a meal.

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